Notice of Allowability	Application No.	Applicant(s)	
	10/769,695	SHARMA ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *8/28/07*.

2. ☒ The allowed claim(s) is/are *1-3,5-10,12-15,18-22,24-27 and 30-33*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-3, 5-10, 12-15, 18-22, 24-27 and 30-41 are pending.

Applicant's amendment filed August 28, 2007 is acknowledged. Applicants' response has been fully considered. Claims 1, 3, 10, 13-15, 22 and 25-27 have been amended. Claims 34-41 are non-elected inventions and withdrawn from consideration. Therefore, claims 1-3, 5-10, 12-15, 18-22, 24-27 and 30-33 are examined.

Withdrawn Claim Rejections - 35 USC § 112

2. The previous rejection of claims 1-3, 5-10, 12-15, 18-22, 24-27 and 30-33 under 35 U.S.C.112, second paragraph, is withdrawn in view of applicants' amendment to the claims, and applicant's response at page 11 in the amendment filed August 28, 2007.

Withdrawn Claim Rejections - Obviousness Type Double Patenting

3. The previous rejection of claims 1-3, 5-10, 12-15, 18-22, 24-27 and 30-33 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5-21, 23, 24, 26-40, 42-56 and 58-76 of co-pending Application No. 10/464,117, is withdrawn in view of applicant's submission of a terminal disclaimer, and applicant's response at pages 11-12 in the amendment filed August 28, 2007.

Examiner's Amendment

An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Stephen A. Slusher on November 9, 2007.

Examiner's Amendment to the Claims:

Cancel claims 34-41.

Claims 1, 3, 10, 12-15, 22 and 24-27 have been amended as follows:

1. (Currently amended) A method of determining the specific residues binding to a target of interest, such residues being within a known parent polypeptide that binds to the target of interest, comprising the steps of:

(a) providing a known parent polypeptide with a known primary structure, such primary structure consisting of n residues where n is 3 to about 20 amino acid residues, which parent polypeptide binds to a target of interest;

(b) constructing a first peptide of the formula R_1-Z-R_2,

wherein

R_1 comprises from 2 to n residues, such residues <u>being</u> the same as residues in the parent polypeptide and in the same order as residues in the parent polypeptide primary structure, provided that any proline residue in the two residue positions immediately adjacent the amino-terminus side of Z is substituted with glycine, alanine, serine, ~~amino isobutyric acid~~ <u>2-aminoisobutyric acid (Aib)</u>, 1-amino, 1-cyclopentane carboxylic acid, or dehydroalanine, and any cysteine residue in R_1 is S-protected or substituted with glycine, alanine, serine, ~~amino isobutyric acid~~ <u>2-aminoisobutyric acid</u>, 1-amino, l-cyclopentane carboxylic acid, or dehydroalanine;

Z is an amino acid residue providing both a nitrogen atom (N) and a sulfur atom (S) for metal ion complexation;

R_2 comprises from 0 to n - 2 residues, such residues <u>being</u> the same as residues in the parent polypeptide and in the same order as residues in the parent polypeptide primary structure, provided that any cysteine residue is S-protected or substituted with glycine, alanine, serine, ~~amino isobutyric acid~~ <u>2-aminoisobutyric acid</u>, 1-amino, 1-cyclopentane carboxylic acid, or dehydroalanine, and forming with R_1 a sequence in the same order as in the parent polypeptide primary structure with Z either inserted between two adjacent residues corresponding to two adjacent residues in such primary structure or substituting for a single

residue corresponding to a single residue in such primary structure, and wherein the residues comprising R_1-Z-R_2 are equal to either n or n +1;

(c) complexing the first peptide of the formula R_1-Z-R_2 to a rhenium (Re) or technetium (Tc) metal ion, thereby forming a first R_1-Z-R_2 metallopeptide;

(d) screening the first R_1-Z-R_2 metallopeptide for binding to the target of interest;

(e) repeating steps (b) through (d), wherein the resulting R_1-Z-R_2 metallopeptide differs in at least either R_1 or R_2; and

(f) selecting the R_1-Z-R_2 metallopeptide exhibiting decreased binding to the target of interest as compared to the binding of the parent polypeptide to the target of interest, whereby at least one residue of the sequence binding to the metal ion of such R_1-Z-R_2 metallopeptide ~~comprises the identification of~~ is identified as the specific residues of the parent polypeptide binding to the target of interest.

3. (Currently amended.) The method of claim 2 wherein the L- or D-3-mercapto amino acid is L- or D-cysteine, or L- or D-penicillamine~~, or 3-mercapto phenylalanine~~.

10. (Currently amended) A method of determining the specific residues binding to a target of interest within a known ~~primary sequence~~ parent polypeptide that binds to the target of interest, comprising the steps of:

(a) providing a parent polypeptide with a known primary sequence consisting of from three to about twenty amino acid residues;

(b) making a series of peptides, wherein each peptide in the series includes the known primary sequence of the parent polypeptide and a single inserted L- or D-3-mercapto amino acid residue, with the single L- or D-3-mercapto amino acid inserted for each peptide at each position along the primary sequence from the position between the second and third residues from the N-terminus through the C-terminus position;

(c) complexing each peptide in the series with a rhenium or technetium metal ion to form a series of metallopeptides;

(d) determining the binding of each metallopeptide of the series of metallopeptides to the target of interest;

(e) selecting the metallopeptide or metallopeptides of the series exhibiting decreased binding to the target of interest as compared to the binding of the parent polypeptide to the target of interest; and

(f) identifying the amino acid residues involved in rhenium or technetium metal ion complexation other than the inserted L- or D-3-mercapto amino acid residue;

whereby at least one of the identified amino acid residues involved in rhenium or technetium metal ion complexation ~~comprises one or more of~~ is the specific residues binding to a target of interest within the known ~~primary sequence~~ parent polypeptide that binds to the target of interest.

12. (Currently amended.) The method of claim 10, wherein any L- or D-3-mercapto amino acid residue in the series of peptides other than the single inserted L- or D-3-mercapto amino acid residue ~~further comprises~~ is modified with a sulfur protecting group, whereby the sulfur therein cannot complex a metal ion.

13. (Currently amended) The method of claim 10, wherein any L- or D-3-mercapto amino acid residue in the series of peptides other than the single inserted L- or D-3-mercapto amino acid residue is substituted with glycine, alanine, serine, ~~amino isobutyric acid~~ 2-aminoisobutyric acid,1-amino, l-cyclopentane carboxylic acid, or dehydroalanine.

14. (Currently amended) The method of claim 10, wherein for any peptide in the series containing a proline residue ~~as~~ in either of the two residues on the immediately adjacent N-terminus side of the single inserted L- or D-3-mercapto amino acid residue, the proline residue is substituted with glycine, alanine, serine, ~~amino isobutyric acid~~ 2-aminoisobutyric acid, 1-amino, 1-cyclopentane carboxylic acid, or dehydroalanine.

15. (Currently amended.) The method of claim 10 wherein the L- or D-3-mercapto amino acid is L- or D-cysteine, or L- or D-penicillamine~~, or 3-mercapto phenylalanine~~.

22. (Currently amended) A method of determining the specific residues binding to a target of interest within a known ~~primary sequence~~ parent polypeptide that binds to the target of interest, comprising the steps of:

(a) providing a parent polypeptide with a known primary sequence consisting of from three to about twenty amino acid residues;

(b) making a series of peptides, wherein each peptide in the series includes the known primary sequence of the parent polypeptide with a single substitution, the single substituent consisting of an L- or D-3-mercapto amino acid residue substituted at each position along the primary sequence from the third residue from the N-terminus through the C-terminus residue;

(c) complexing each peptide in the series with a rhenium or technetium metal ion to form a series of metallopeptides;

(d) determining the binding of each metallopeptide of the series of metallopeptides to the target of interest;

(e) selecting the metallopeptide or metallopeptides of the series exhibiting decreased binding to the target of interest as compared to the binding of the parent polypeptide to the target of interest; and

(f) identifying the amino acid residues involved in rhenium or technetium metal ion complexation;

whereby at least one of the identified amino acid residues involved in rhenium or technetium metal ion complexation and/or the amino acid residue substituted with an L- or D-3-mercaptoamino acid residue ~~comprises one or more of~~ are the specific residues binding to a target of interest within the known ~~primary sequence~~ parent polypeptide that binds to the target of interest.

24. (Currently amended.) The method of claim 22, wherein any L- or D-3-mercapto amino acid residue in the series of peptides other than the single substituent L- or D-3-mercapto amino acid residue ~~further comprises~~ is modified with a sulfur protecting group, whereby the sulfur therein cannot complex a metal ion.

25. (Currently amended) The method of claim 22, wherein any L- or D-3-mercapto amino acid residue in the series of peptides other than the single substituent L- or D-3-mercapto amino acid residue is substituted with glycine, alanine, serine, ~~amino isobutyric acid~~ 2-aminoisobutyric acid,1-amino, l-cyclopentane carboxylic acid, or dehydroalanine.

26. (Currently amended) The method of claim 22, wherein for any peptide in the series containing a proline residue ~~as~~ in either of the two residues on the immediately adjacent N-terminus side of the single substituent L- or D-3-mercapto amino acid residue, the proline residue is substituted with glycine, alanine, serine, ~~amino isobutyric acid~~ 2-aminoisobutyric acid, 1-amino, 1-cyclopentane carboxylic acid, or dehydroalanine.

27. (Currently amended.) The method of claim 22 wherein the L- or D-3-mercapto amino acid is L- or D-cysteine, or L- or D-penicillamine~~, or 3-mercapto phenylalanine~~.

The following is an **Examiner's Statement of Reasons for Allowance**: The following reference appears to be related to the claimed invention. Sharma *et al.* (US2002/0012948, filed 6/14/2001) disclose metallopeptide combinatorial libraries and their use for screening those metallopeptides having desired specificity and affinity. However, the reference does not teach or suggest the use of a series of metallopeptides by inserting an amino acid residue having a nitrogen atom and a sulfur atom to form metal ion complexation (i.e., Cys) or substituting an amino acid having a nitrogen atom and a sulfur atom at various positions of a known polypeptide to identify the specific residues of the known polypeptide that bind to a target of interest. Therefore, the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

CHIH-MIN KAM
PRIMARY EXAMINER

CMK
November 9, 2007